Malignant Melanoma Associated with Pregnancy.

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More than a thousand cases of malignant melanoma have been observed and treated in the Memorial Hospital and in other hospitals by the staff of the Pack Medical Group during the past thirty-two years (since 1917). The primary melanomas are located on all parts of the body integument, including the skin, palms of hands, soles of feet and nail beds. In addition, there are malignant melanomas involving the paranasal sinuses, oral mucosa, anus and rectum, meninges, and choroid of the eye.

We have been especially interested in studying the hormonal influences on pigmented tumors. The development of pigmented nevi at puberty is well known, and the peculiar benign nature of pre-pubertal or juvenile melanomas in young children, in spite of their malignant histological structure, has been made a subject of special study.

Pregnancy is another period of altered hormone balance when many temporary and permanent pigmentations of the skin develop. There is often growth of a pre-existing pigmented nevus, fortunately not always to a malignant melanoma, as we have proved by excising them for histologic study. In 28 of our patients with malignant melanoma, however, the melanoma has seemed to develop in a pre-existing nevus during pregnancy, or else a pregnancy has come in a patient with malignant melanoma and has hastened the growth. Eight of our 28 patients with malignant melanoma gave history of the growth of a pre-existing pigmented tumor during pregnancy. Ten others presented themselves for treatment during the pregnancy with the malignant melanoma present and in some stage of development.

We both remember very graphically a young 28-year-old woman who very early in the course of her disease presented a picture of a very advanced melanomatosis, showing multiple dark blue-black cutaneous nodules in the region of the right chest wall, shoulder, arm and back. This young woman was in the fifth month of her pregnancy when she noticed the small lesion on the back in the right scapular region, which became red and sore. She visited a local hospital about a month later, where it was removed by a small excision, leaving a scar 3 cm. long. About four weeks later it grew back in the scar and she called attention to it when reporting for prenatal care. It was again removed with a skin segment about twice as big as the first. When she reached the eighth month of gestation, the pregnancy was interrupted by bag induction. A normal five-pound baby was delivered spontaneously. About a month later, a radical right axillary dissection was done and the specimen showed extensive metastases in the lymph nodes. Four months later, and eight months after the original excision, the multiple skin nodules appeared and the skin of the face and chest had a bluish cast. There were numerous shiny blue-black nodules and marked melanuria. She did not yet have demonstrable visceral metastases, but a few months later the spleen was markedly enlarged and very hard. When she died, sixteen months after her admission to us and fourteen months after the delivery, postmortem examination showed the most extensive cutaneous, subcutaneous and visceral involvement that one can imagine. Black nodules studded absolutely all the tissues.

The end-result has been fatal in fourteen, or 50%, of these patients, in three years or less. Of the patients treated over five years ago, only three survived, and only two are known to live over a five-year period, as one was lost to observation after four years. Those two are living eight and thirteen years, respectively, and are considered cured. One patient has had two normal pregnancies and deliveries at a safe interval after the radical surgical removal of the malignant melanoma which had not metastasized to the regional lymph nodes when they were dissected out.

All the patients treated within fairly recent years have had radical surgical treatment, including not only the wide excision of the site of the primary melanoma, but dissection continuously to the regional lymph nodes and radical removal of the lymph-node-bearing area. A 35-year-old woman may be used to illustrate this method of treatment. She presented herself for treatment with a lesion on the back and giving the following history: For four years she noticed something on her back. Four months before, while she was pregnant, it began to ulcerate and have a discharge. She consulted her family physician, who removed it by electrodesiccation. It grew back within a month. The following month she delivered a normal child. When we saw her, she had a raised, firm, bluish to brown growth 10 by 15 mm. in the margin of a scar situated in the midline of the back between the scapulae. At that time she had two small lymph nodes palpable in one axilla and larger hard ones in the opposite one. The malignant melanoma on the back was excised with a skin segment 5 to 6 cm. wide above and below and extending continuously to the axilla on each side. The subcutaneous fat and fascia over the muscles were removed more widely across the back and to each axilla. The axillary veins were dissected free of all fat and lymphoid tissue up to a level behind the pectoralis minor muscle. The axillary tissue on either side was removed in continuity with the tissue from the back. The microscopical examination confirmed the clinical diagnosis of metastatic melanoma in the lymph nodes from both axillae. In spite of this very radical surgery, a year later this patient had palpable hard nodules in both breasts. Both breasts were removed completely and there were two masses representing metastatic

melanoma in the right one and five in the left breast. Metastatic nodules next made their appearance in the neck and then in the liver, and in less than two years after her delivery and treatment, she died of malignant disease.

We have eleven patients in this series living and well at the present time, but most of them have been operated upon within the past two years.

These original observations are clinical, but may be summarized as follows:

(1) The benign or premelanotic nevus is definitely stimulated by hormonal changes of puberty and pregnancy.

(2) Pre-pubertal melanomas possessing all the histologic features of malignant melanoma except blood and lymph vessel invasion do not metastasize until puberty (with rare exception).

(3) Certain benign nevi are prone to change to malignant melanoma during pregnancy.

(4) Malignant melanomas grow with great rapidity, metastasize early and widely, are more malignant and have a lower rate of curability during pregnancy.

(5) Dormant, silent, residual melanoma may flare into active recurrence during pregnancy, subsequent to operative removal.

(6) Prophylaxis is removal of all suspicious nevi in women before or at least early during pregnancy.

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Questions of HERMAN CHARACHE,
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1. In your experience with over one thousand cases of malignant melanoma, did you find whether melanuria is of any prognostic value?

Answer: We believe that melanuria is very frequently present in cases of malignant melanoma. There are other conditions also in which this reaction may be demonstrated. We do not believe that it has any important prognostic value.

2. Is the color of pigmented nevi, such as black, brown or blue, of any prognostic significance?

Answer: It has long been our practice to excise all blue-black moles, no matter how benign they appear. Of course many of these moles are Jadassohn neuronevi. These nevi are considered not to undergo malignant degeneration very often, but we have cases in which it has occurred. Otherwise, there is no great significance in the color of the moles, as a certain percentage of malignant melanomas contain no pigmentation at all. These non-pigmented melanomas may, however, produce pigmented metastases in lymph nodes. The color, therefore, has no great prognostic significance.

3. Would you recommend sterilization of young women with malignant melanoma, or interrupt early pregnancy in women with malignant melanomas?

Answer: The sterilization of young women with malignant melanoma seems to us a rather drastic procedure, as we believe that with radical surgery in early stages, we are able to cure these patients. I have cited one case where a woman is living and well for thirteen years and has had two normal pregnancies with deliveries since her malignant melanoma was treated, although it developed during the course of her first pregnancy. This woman had a spontaneous interruption of the first pregnancy, and I personally believe that if the malignant melanoma is diagnosed early enough in pregnancy so that therapeutic abortion can be carried out safely, it should be done.

Benign and Malignant Neoplasia of Melanoblasts Through the Eyes of the Dermatologist.

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Benign neoplasia of melanoblasts (1) is seen in prenatal pigmented nevi, which are either present at birth or appear during the first few years of life. Human beings average 18 to 20 such lesions (Pack). They vary from small macules to large, elevated, nonhairy or hairy plaques. Most nevi are pigmented; a few small elevated lesions are non-pigmented, especially on the face and scalp.

Acquired nevi appear in late childhood or early adult life in the form of flesh-